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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,103	12/10/2001	Anthony Boey	20801-000810	3038
20350	7590	06/25/2004	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER EIGHTH FLOOR SAN FRANCISCO, CA 94111-3834			KISHORE, GOLLAMUDI S	
			ART UNIT	PAPER NUMBER
			1615	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,103	BOEY ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-66 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-66 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims included in the prosecution are 1-66.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 11, 41, 58 and 64-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether the diameters recited in claims 11, 41 and 58 pertain to the complex or the liposomes. Clarification is requested.

'said PEG-ceramide' lacks in claim 64 an antecedent basis.

Claims 65-66 refer back to claim 55 and recite step c of claim 55. There is no step c in claim 55.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-4, 8, 15, 26-27, 32-35, 39, 43, 55 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/34647 of record.

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WO 95 discloses liposomal compositions containing nucleic acid wherein the nucleic acid is in a complex form with a histone protein and a method of transfection. The liposomes are either anionic or cationic. The compositions further contain asialoorosomucoid (bilayer stabilizing agent) (abstract, pages 2, 3, 7, 10, 11, Examples and claims).

5. Claims 1-8, 12-17, 21-22, 26-39, 42-45, 49, 52-53, 55, 57-58, 62-63 and 65-66 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/20857 of record.

WO 98 discloses liposomal formulations containing nucleic acid complexes and a method of transfection. The nucleic acid is reacted with an organic polycation (spermidine, spermine) to produce a condensed nucleic acid. The composition is further stabilized by the addition of a hydrophilic polymer (PEG). The phospholipids taught by WO include phosphatidic acid, phosphatidylcholine, phosphatidyl inositol, and dioleoylphosphatidylethanolamine. The liposomes are unilamellar and sizes encompassing the instant sizes. PEG used in the compositions has a molecular weight of 1,000 to 10,000 Daltons. The liposomes are prepared by using the standard methods of liposomes including detergent dialysis and reverse phase evaporation (abstract, pages 3-4, 7-9, 12, 16-17, 22-25, Examples and claims).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 11-14, 23-31, 41-42, 49-53, 56, 58, 62-63 and 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/20857 cited above.

The teachings of WO 98 have been discussed above. As pointed out above, WO 98 teaches the liposomes of sizes which encompass instant sizes. Furthermore, on page 24, WO teaches that several techniques are available to prepare liposomes of less than 0.05 microns if desired, and therefore, in the absence of showing the criticality, the preparation of different desired sizes of liposomes is deemed to be within the skill of the art. WO expresses the ratios of the polycation to the nucleic acid in terms of n moles per microgram of nucleic acid. Assuming the ratios are different from instant ratios, it is deemed obvious to vary the amounts of the nucleic acid since this depends on the nature of the treatment using the composition. WO does not teach all of the claimed mole percentages of PEG; however, since PEG is taught as a bilayer stabilizer compound, one of ordinary skill in the art would be motivated to vary the amounts to obtain the best possible stabilization effect based on the guidance provided by WO. WO does not provide examples of the preparation of liposomes using detergent dialysis and ethanol injection. However, since these are art well-known methods, it is deemed obvious for one skilled in the art to choose a suitable method of preparation with a reasonable expectation of success. The criticality of adding two condensing agents, that too, the same agent two times, is not readily apparent to the examiner in the absence of comparative studies.

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8. Claims 17-20, 28-29, 45-48, 53-54, 60 and 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/34647 or WO 98/20857 cited above, further in view of Holland (5,885,613).

The teachings of WO 95 and WO 98 have been discussed above. What is lacking in these references is the teaching of PEG ceramide as the bilayer-stabilizing component. What are also lacking in these references are the explicit teachings of the molecular weights of PEG and PEG-lipid amounts in molar percentages.

Holland while disclosing liposomal compositions for the delivery of nucleic acids teaches that PEG when attached to phosphatidylethanolamine (PE) or ceramide (C 14-C20 ceramides) stabilizes the bilayer. The molecular weight range of PEG is 200-10,000 and the amount of the PEG-lipid is in the range of 0.05 to 30 mole percent (abstract, col. 8, line 60 through col. 9, line 57, col. 24, line 4 through col. 25, line 46 and claims).

The use of PEG-ceramide as the PEG lipid instead of PEG-PE would have been obvious to one of ordinary skill in the art since Holland teaches the effectiveness of both PEG-PE and PEG-ceramide in liposome compositions used in the delivery of nucleic acids. Choosing the appropriate amounts of PEG-lipid and PEG with desired molecular weight with a reasonable expectation of success would have been obvious to one of ordinary skill in the art since Holland teaches manipulations with these parameters.

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9. Claims 8-10, 23-25, 39-40, 50-51 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/34647 or WO 98/20857 cited above, further in view of Lisziewicz (6,420,176).

The teachings of WO 95 and WO 98 have been discussed above. What are lacking in these references are the teachings of the use of polyethylenimine as the polycation or the condensing agent.

Lisziewicz while disclosing compositions for delivering DNA into cells teaches that the cationic polymer, polyethylenimine (PEI 25 kD) is effective in binding to DNA and makes a complex and this complex can enter into endosomes of the skin's antigen presenting cells, Langerhans cells, via asialoglycoprotein receptor-mediated endocytosis (abstract, col. 10, line 24 et seq., and claims).

The use of PEI as the polycation in the teachings of WO 95 or WO 98 with a reasonable expectation of success since Lisziewicz teaches the ability of this polycation to bind to DNA and effectively enter into endosomes of the skin's antigen presenting cells, Langerhans cells, via asialoglycoprotein receptor-mediated endocytosis.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone

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number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK